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Chapter 44: Sexually Transmitted Infections

INTRODUCTION

- *Definition*: The spectrum of sexually transmitted infections (STIs) includes the classic venereal diseases—gonorrhea, syphilis, chancroid, lymphogranuloma venereum, and granuloma inguinale—as well as a variety of other pathogens known to be spread by sexual contact (**Table 44-1**). Selected clinical syndromes associated with STIs are listed in **Table 44-2**. The most current information on epidemiology, diagnosis, and treatment of STIs provided by the Centers for Disease Control and Prevention (CDC) can be found at www.cdc.gov.

TABLE 44-1

Sexually Transmitted Infections

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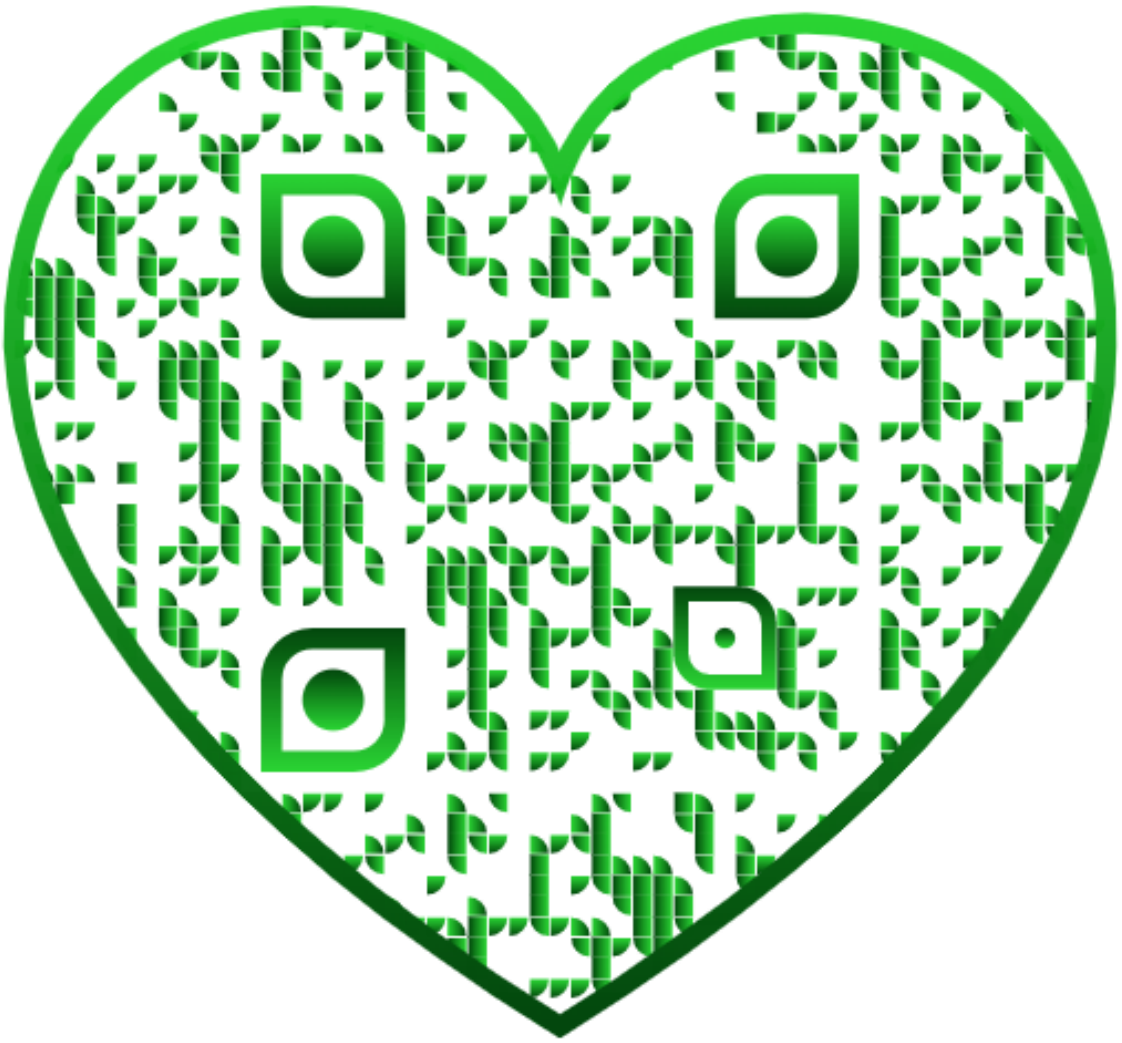

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Disease	Associated Pathogens
Bacterial	
Gonorrhea	*Neisseria gonorrhoeae*
Syphilis	*Treponema pallidum*
Chancroid	*Haemophilus ducreyi*
Granuloma inguinale	*Klebsiella granulomatis*
Enteric disease	*Salmonella* spp., *Shigella* spp., *Campylobacter fetus*
Campylobacter infection	*Campylobacter jejuni*
Bacterial vaginosis	*Gardnerella vaginalis*, *Mycoplasma hominis*, *Bacteroides* spp., *Mobiluncus* spp.
Chlamydial	
Nongonococcal urethritis	*Chlamydia trachomatis*
Lymphogranuloma venereum	*C. trachomatis*, type L
Viral	
Acquired immunodeficiency syndrome	Human immunodeficiency virus
Herpes genitalis	Herpes simplex virus, types 1 and 2
Viral hepatitis	Hepatitis A, B, C, and D viruses
Condylomata acuminata	Human papillomavirus
Molluscum contagiosum	Poxvirus
Mycoplasmal	
Nongonococcal urethritis	*Mycoplasma genitalium*
Protozoal	
Trichomoniasis	*Trichomonas vaginalis*
Fungal	
Vaginal candidiasis	*Candida albicans*

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TABLE 44-2

Selected Syndromes Associated with Common Sexually Transmitted Pathogens

Syndrome	Commonly Implicated Pathogens	Common Clinical Manifestations[a]
Urethritis	*C. trachomatis*, herpes simplex virus, *N. gonorrhoeae*, *T. vaginalis*, *Ureaplasma urealyticum*, *M. genitalium*	Urethral discharge, dysuria
Epididymitis	*C. trachomatis*, *N. gonorrhoeae*, Enterobacterales	Scrotal pain, inguinal pain, flank pain, urethral discharge
Cervicitis/vulvovaginitis	*C. trachomatis*, *G. vaginalis*, herpes simplex virus, human papillomavirus, *N. gonorrhoeae*, *T. vaginalis*	Abnormal vaginal discharge, vulvar itching/irritation, dysuria, dyspareunia
Genital ulcers (painful)	*H. ducreyi*, herpes simplex virus	Usually multiple vesicular/pustular (herpes) or papular/pustular (*H. ducreyi*) lesions that can coalesce; painful, tender lymphadenopathy[b]
Genital ulcers (painless)	*T. pallidum*	Usually single papular lesion
Genital/Anal warts	Human papillomavirus	Multiple lesions ranging in size from small papular warts to large exophytic condylomas
Pharyngitis	*C. trachomatis*, herpes simplex virus, *N. gonorrhoeae*	Symptoms of acute pharyngitis, cervical lymphadenopathy, fever[c]
Proctitis	*C. trachomatis*, herpes simplex virus, *N. gonorrhoeae*, *T. pallidum*	Constipation, anorectal discomfort, tenesmus, mucopurulent rectal discharge
Salpingitis	*C. trachomatis, N. gonorrhoeae*	Lower abdominal pain, purulent cervical or vaginal discharge, adnexal swelling, fever[d]
Skin rash or lesions, with or without constitutional symptoms	*T. pallidum*, herpes simplex virus, mpox virus, *N. gonorrhoeae*	Variety of presentations (esp. *T. pallidum*), including extent of disease (local or disseminated), systemic manifestations (fever, lymphadenopathy)

[a]For some syndromes, clinical manifestations can be minimal or absent.

[b]Recurrent herpes infection can manifest as a single lesion.

[c]Most cases of pharyngeal gonococcal infection are asymptomatic.

[d]Salpingitis increases the risk of subsequent ectopic pregnancy and infertility.

GONORRHEA

- *N. gonorrhoeae* is a gram-negative diplococcus; 710,151 cases were reported to the CDC in 2021. Humans are the only known host of this

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intracellular parasite.

- Drug-resistant *N. gonorrhoeae* continues to pose a serious health threat requiring urgent and aggressive action and about half of all infections in 2022 were estimated to harbor resistance to at least one antibiotic.

CLINICAL PRESENTATION

- Infected individuals may be symptomatic or asymptomatic, have complicated or uncomplicated infections, and have infections involving several anatomical sites. The majority of women diagnosed with gonorrhea are asymptomatic.
- The most common clinical features of gonococcal infections are presented below.

  ✓ Incubation period: 1–14 days, symptom onset in 2–8 days (males) and 10 days (females).

  ✓ Most common site of infection: Urethra (males), endocervical canal (females); other sites: rectum (usually caused by rectal intercourse in men who have sex with men [MSM]), oropharynx, eye (males) and urethra, rectum (usually caused by perineal contamination), oropharynx, eye (females).

  ✓ Symptoms

  - Males: Commonly symptomatic, may be asymptomatic; urethral infection: dysuria and urinary frequency; anorectal infection: asymptomatic to severe rectal pain; pharyngeal infection: asymptomatic to mild pharyngitis.
  - Females: Can be asymptomatic or minimally symptomatic; endocervical infection: usually asymptomatic or mildly symptomatic; urethral infection: dysuria, urinary frequency; anorectal and pharyngeal infection; symptoms same as for men.

  ✓ Signs: Purulent urethral or rectal discharge can be scant to profuse; anorectal: pruritus, mucopurulent discharge, bleeding (males) and abnormal vaginal discharge or uterine bleeding; purulent urethral or rectal discharge can be scant to profuse (females).

  ✓ Complications: Rare (epididymitis, prostatitis, inguinal lymphadenopathy, urethral stricture) in males; pelvic inflammatory disease (PID) and associated complications (ie, ectopic pregnancy, infertility) in females.
- Ninety percent of males experience symptoms within 2–6 days following exposure, most commonly mucopurulent penile discharge and dysuria. Approximately 10%–20% of women with gonorrhea develop PID. Left untreated, PID can be an indirect cause of infertility and ectopic pregnancies.
- In 0.5%–3% of patients with gonorrhea, the gonococci invade the bloodstream and produce disseminated disease. The usual clinical manifestations of disseminated gonococcal infection (DGI) are tender necrotic skin lesions, tenosynovitis, and monoarticular arthritis.
- Diagnosis of gonococcal infections can be made by gram-stained smears, culture, or detection of cellular components (eg, enzymes, antigens, or DNA).
- Nucleic acid amplification techniques (NAATs) have replaced culture in most settings as the primary diagnostic or screening test.
- The CDC and US Preventative Services Task Force recommend routine annual screening for gonococcal infection for all sexually active women younger than 25.

TREATMENT

- Goals of Treatment: Resolution of infection without complications or reinfection or recurrence.
- A single 500-mg intramuscular (IM) ceftriaxone dose is recommended for treatment of uncomplicated gonococcal infections (**Table 44-3**). Patients weighing 150 kg or more should receive ceftriaxone 1 g. An 800-mg oral dose of **cefixime** may be substituted if ceftriaxone is unavailable.
- Because coexisting chlamydial infections are common, chlamydia treatment should be added with doxycycline 100 mg orally twice daily for 7 days.
- Intravenous (IV) ceftriaxone is the recommended therapy for DGI, including meningitis and endocarditis, and any type of gonococcal infection in

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children.

- Pregnant females infected with *N. gonorrhoeae* should be treated with a single IM dose of ceftriaxone 500 mg, with the addition of 1 g of oral azithromycin if chlamydia has not been ruled out.
- Treatment of gonorrhea during pregnancy is essential to prevent ophthalmia neonatorum. The CDC recommends that **erythromycin (0.5%) ophthalmic ointment** be instilled in each conjunctival sac immediately postpartum to prevent ophthalmia neonatorum.
- The CDC recommends all treatment failures receive culture and sensitivity testing.

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TABLE 44-3

Treatment of Gonorrhea

Type of Infection	Recommended Regimens[a]	Alternative Regimens[a]
Uncomplicated infections of the cervix, urethra, and rectum in adults	Ceftriaxone 500 mg IM once[b,c]	Gentamicin 240 mg IM[d] *plus* Azithromycin 2 g orally once *or* When ceftriaxone administration is not feasible, cefixime 800 mg orally once[c]
Uncomplicated infections of the pharynx	Ceftriaxone 500 mg IM once[b,c]	Consult with infectious disease expert
DGI in adults (>45 kg)	Ceftriaxone 1–2 g IM or IV every 12–24 hours[c,e]	Cefotaxime 1 g IV every 8 hours[c,e] or ceftizoxime 1 g IV every 8 hours[c,e]
Gonococcal conjunctivitis in adults	Ceftriaxone 1 g IM once[f]	
Ophthalmia neonatorum	Ceftriaxone 25–50 mg/kg IV or IM once (not to exceed 250 mg)	
Infants born to mothers with gonococcal infection (prophylaxis)	Erythromycin (0.5%) ophthalmic ointment in a single application[g] Ceftriaxone 25–50 mg/kg IM or IV once (not to exceed 125 mg)	

[a]Recommendations are those of the CDC.

[b]For patients weighing >150 kg, a 1-g dose of ceftriaxone is recommended.

[c]If chlamydial infection cannot be ruled out, treatment for chlamydia should be administered. Preferred therapy is doxycycline 100 mg orally twice daily × 7 days. Azithromycin 1 g orally once may be used as an alternative. Tetracyclines are contraindicated during pregnancy. Pregnant women should be treated with recommended cephalosporin-based combination therapy. In severe cephalosporin allergy, consultation with an infectious diseases expert is recommended.

[d]For patients with severe cephalosporin allergy.

[e]Parenteral treatment duration should be determined in consultation with an infectious diseases expert. Gonococcal meningitis should be treated with ceftriaxone 2 g IV every 12 hours. Parenteral therapy for meningitis should be continued for at least 10–14 days and at least 4 weeks in endocarditis.

[f]A single lavage of the infected eye with normal saline should be considered; empiric therapy for *C. trachomatis* is recommended.

[g]Efficacy in preventing chlamydial ophthalmia is unclear.

SYPHILIS

- The causative organism of syphilis is *T. pallidum*, a spirochete.

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- Syphilis is usually acquired by sexual contact with infected mucous membranes or cutaneous lesions, although on rare occasions it can be acquired by nonsexual personal contact, accidental inoculation, or blood transfusion. Rates of coinfection with HIV have remained high, particularly among MSM.

CLINICAL PRESENTATION AND DIAGNOSIS

- The clinical presentation of syphilis is varied, with progression through multiple stages possible in untreated or inadequately treated patients.
- Serologic tests are the mainstay in the diagnosis of syphilis and are categorized as nontreponemal or treponemal. Common nontreponemal tests include the Venereal Disease Research Laboratory (VDRL) slide test and rapid plasma reagin (RPR) card test.
- Treponemal tests are more sensitive than nontreponemal tests and are used to confirm the diagnosis (ie, the fluorescent treponemal antibody absorption).

Primary Syphilis

- Primary syphilis is characterized by the appearance of a chancre on cutaneous or mucocutaneous tissue exposed to the organism and is highly infectious. Chancres heal within 4–6 weeks, although lymphadenopathy may persist longer.
- Incubation period: 10–90 days (mean, 21 days).
- Site of infection: External genitalia, perianal region, mouth, and throat.
- Signs and symptoms: Single, painless, indurated lesion (chancre) that erodes, ulcerates, and eventually heals (typical); regional lymphadenopathy is common; multiple, painful, purulent lesions possible.

Secondary Syphilis

- The secondary stage of syphilis is characterized by a variety of mucocutaneous eruptions, resulting from widespread hematogenous and lymphatic spread of *T. pallidum.* There is multisystem involvement secondary to hematogenous and lymphatic spread.
- Develops 2–8 weeks after initial infection in untreated or inadequately treated individuals.
- Skin lesions are often maculopapular and are usually nonpruritic, developing first on trunk and proximal arms and disseminating bilaterally. Secondary syphilis lesions typically involve the palms and soles, can present as mucous patches, and/or can have a wart-like appearance (condylomata lata). Patchy alopecia is another finding periodically seen.
- If untreated, secondary syphilis disappears spontaneously within 1–6 months.

Latent Syphilis

- Develops 4–10 weeks after the secondary stage in untreated or inadequately treated individuals; risk of secondary stage relapse within the first year.
- Persons with a positive serologic test for syphilis but with no other evidence of disease have latent syphilis.
- If left untreated, syphilis can slowly produce an inflammatory reaction in virtually any organ in the body. Most patients with late syphilis will have no further sequelae. However, approximately 28% will develop further disease years after the initial infection.

Tertiary Syphilis and Neurosyphilis

- Develops in approximately 28% of untreated or inadequately treated individuals 10–30 years after initial infection. Neurologic manifestations, including ocular and otic, cardiovascular syphilis (aortitis or aortic insufficiency), and gummatous lesions involving any organ or tissue may present.

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- Gummas, nonspecific granulomatous lesions, are the classic lesions of late syphilis and can infiltrate any organ or tissue.

TREATMENT

- Goals of Treatment: Resolution of infection and prevention of medical complications. Also, to prevent spread of infection including to the newborn. Treatment recommendations from the CDC for syphilis are presented in **Table 44-4**. Parenteral penicillin G is the treatment of choice for all stages of syphilis. **Benzathine penicillin G** is the only penicillin effective for single-dose therapy. The recommended treatment for syphilis of less than 1 year's duration is benzathine penicillin G 2.4 million units as a single IM dose.
- Alternative regimens recommended for penicillin-allergic patients are **doxycycline** 100 mg orally twice daily or **tetracycline** 500 mg orally four times daily for 2–4 weeks depending on the duration of syphilis infection.
- For pregnant patients, penicillin is the treatment of choice at the dosage recommended for that particular stage of syphilis. To ensure treatment success and prevent transmission to the fetus, some experts advocate an additional IM dose of benzathine penicillin G, 2.4 million units, 1 week after completion of the recommended regimen.
- Patients treated for primary and secondary syphilis experience the Jarisch–Herxheimer reaction after treatment, characterized by flu-like symptoms such as transient headache, fever, chills, malaise, arthralgia, myalgia, tachypnea, peripheral vasodilation, and aggravation of syphilitic lesions. The Jarisch–Herxheimer reaction should not be confused with penicillin allergy. Most reactions can be managed symptomatically with analgesics, antipyretics, and rest.
- The CDC recommendations for serologic follow-up of patients treated for syphilis are given in **Table 44-4**. Quantitative nontreponemal tests should be performed at 6 and 12 months in all patients treated for primary and secondary syphilis and at 6, 12, and 24 months for early and late latent disease.
- For women treated during pregnancy, monthly, quantitative, nontreponemal tests are recommended in those at high risk of reinfection.

TABLE 44-4

Drug Therapy and Follow-up of Syphilis

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Stage/Type of Syphilis	Recommended Regimens[a,b]	Follow-up Serology
Primary, secondary, or early latent syphilis (<1 year's duration)	Adults: benzathine penicillin G 2.4 million units IM in a single dose Children: Benzathine penicillin G 50,000 units/kg IM in a single dose, up to 2.4 million units	Quantitative nontreponemal tests at 6 and 12 months with failure if titer does not decrease at least fourfold in 12 months[c]
Late latent syphilis (>1 year's duration) or latent syphilis of unknown duration or tertiary syphilis or retreatment after failure	Adults: benzathine penicillin G 2.4 million units IM once a week for 3 successive weeks (7.2 million units total) Children: benzathine penicillin G 50,000 units/kg IM once a week for 3 successive weeks, up to 7.2 million units total	Quantitative nontreponemal tests at 6, 12, and 24 months with failure if titer does not increase at least fourfold in 24 months[c]
Neurosyphilis, including ocular or otic involvement	Aqueous crystalline penicillin G 18–24 million units IV (3–4 million units every 4 hours or by continuous infusion) for 10–14 days[d,e] *or* Aqueous procaine penicillin G 2.4 million units IM daily plus probenecid 500 mg orally four times daily, both for 10–14 days	Repeat CSF examination is no longer required at 6 months if adequate RPR response (decrease by fourfold or greater)
Congenital syphilis (infants with proven or highly probable disease)	Aqueous crystalline penicillin G 50,000 units/kg/dose IV every 12 hours during the first 7 days of life and every 8 hours thereafter for a total of 10 days *or* Procaine penicillin G 50,000 units/kg IM daily for 10 days[d]	Serologic follow-up only recommended if antimicrobials other than penicillin are used
Penicillin-Allergic Patients[e,f]		
Primary, secondary, or early latent syphilis	Doxycycline 100 mg orally two times daily for 14 days *or* Tetracycline 500 mg orally four times daily for 14 days *or* Ceftriaxone 1–2 g IM or IV daily for 10–14 days	Same as for non–penicillin-allergic patients
Late latent syphilis (>1 year's duration) or syphilis of unknown duration	Doxycycline 100 mg orally twice a day for 28 days *or* Tetracycline 500 mg orally four times daily for 28 days	Same as for non–penicillin-allergic patients

CDC, Centers for Disease Control and Prevention; CSF, cerebrospinal fluid; HIV, human immunodeficiency virus; RPR, rapid plasma reagin.

[a]Recommendations are those of the CDC.

[b]The CDC recommends that all patients diagnosed with syphilis be tested for HIV infection.

[c] No specific recommendations exist for tertiary syphilis because of the lack of available data.

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[d] Some experts administer benzathine penicillin G 2.4 million units IM once per week for up to 3 weeks after completion of the neurosyphilis regimens to provide a total duration of therapy comparable to that used for late syphilis in the absence of neurosyphilis.

[e] Growing data support ceftriaxone efficacy, although the optimal dosage and treatment duration are unclear; in neurosyphilis, 2 g IV daily for at least 10 days found to be as effective as IV penicillin G.

[f] For nonpregnant patients; pregnant patients should be treated with penicillin after desensitization.

CHLAMYDIA

- Infections caused by *C. trachomatis* are believed to be the most common STI in the United States. *C. trachomatis* is an obligate intracellular parasite that has some similarities to viruses and bacteria.

CLINICAL PRESENTATION

- In comparison with gonorrhea, chlamydial genital infections are more frequently asymptomatic, and when present, symptoms tend to be less noticeable. The usual clinical presentation of chlamydial infections is as follows.
- Incubation period: 7–35 days (males and females).
- Symptom onset: 7–21 days (males and females).
- Most common site of infection: Urethra (males), endocervical canal (females); other sites: rectum (receptive anal intercourse), oropharynx, eye (males), urethra, rectum (usually caused by perineal contamination), oropharynx, eye (females).
- Symptoms:
  - ✓ Males: More than 50% of urethral and rectal infections are asymptomatic; urethral infection: mild dysuria, discharge; pharyngeal infection: asymptomatic to mild pharyngitis.
  - ✓ Females: More than 66% of cervical infections are asymptomatic; urethral infection: usually subclinical; dysuria and frequency uncommon; rectal and pharyngeal infection: symptoms same as for men.
- Signs:
  - ✓ Males: Scant to profuse, mucoid to purulent urethral or rectal discharge; rectal infection: pain, discharge, bleeding.
  - ✓ Females: Abnormal vaginal discharge or uterine bleeding, purulent urethral or rectal discharge can be scant to profuse.
- Complications include epididymitis, Reiter's syndrome (rare) in males, PID and associated complications (ie, ectopic pregnancy, infertility), Reiter's syndrome (rare) in females.
- Chlamydia may be transmitted to an infant during contact with infected cervicovaginal secretions. Nearly two-thirds of infants acquire chlamydial infection after endocervical exposure, with the primary morbidity associated with seeding of the infant's eyes, nasopharynx, rectum, or vagina.
- Culture of endocervical or urethral epithelial cell scrapings is the most specific method for detection of chlamydia, but sensitivity is low. Between 3 and 7 days are required for results.
- Tests that allow rapid identification of chlamydial antigens and nucleic acid provide more rapid results and are technically less demanding to perform, are less costly, and, in some situations, have greater sensitivity than culture. NAATs are the most sensitive tests for first-catch urine, endocervix and vaginal swab specimens in women, and urethral swab specimens in men, and are therefore the recommended tests for detecting chlamydia infection.

TREATMENT

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- Goal of Treatment: Resolution of infection without reinfection.
- Doxycycline 100 mg orally twice daily for 7 days is preferred to **azithromycin** 1 g orally as a single dose for treatment of uncomplicated urogenital chlamydia infections (**Table 44-5**).
- Treatment of chlamydial infections with the recommended regimens is highly effective; therefore, posttreatment cultures are not routinely recommended.
- Infants with pneumonitis should receive follow-up testing because **erythromycin** is only 80% effective.
- For infected pregnant females, azithromycin is the recommended treatment.

TABLE 44-5

Treatment of Chlamydia Infections

Infection	Recommended Regimens[a]	Alternative Regimens[a]
Uncomplicated urethral, endocervical, or rectal infection in adults	Doxycycline 100 mg orally twice daily for 7 days	Azithromycin 1 g orally once,[b] *or* levofloxacin 500 mg orally once daily for 7 days
Urogenital infections during pregnancy	Azithromycin 1 g orally as a single dose	Amoxicillin 500 mg orally three times daily for 7 days
Conjunctivitis of the newborn or pneumonia in infants	Erythromycin base or ethylsuccinate 50 mg/kg/day orally in four divided doses for 14 days[c,d]	Azithromycin suspension 20 mg/kg/day orally once daily for 3 days[c]

[a]Recommendations are those of the CDC.

[b]Azithromycin may be used if there are concerns for nonadherence. Test after treatment is recommended due to reduced efficacy in rectal chlamydia.

[c]An association between oral erythromycin and azithromycin and infantile hypertrophic pyloric stenosis (IHPS) has been reported in infants aged <6 weeks. Infants treated with either of these antimicrobials should be followed for signs and symptoms of IHPS.

[d]Topical therapy alone is inadequate for ophthalmia neonatorum and is unnecessary when systemic therapy is administered. Effectiveness of erythromycin treatment is approximately 80%; therefore, a second course of therapy may be required.

GENITAL HERPES

- The term ***herpes*** is used to describe two distinct but antigenically related serotypes of herpes simplex virus (HSV). HSV type 1 (HSV-1) is most commonly associated with oropharyngeal disease; type 2 (HSV-2) is most closely associated with genital disease.
- First-episode primary infection is when initial genital infection occurs in individuals lacking antibody to either HSV-1 or HSV-2.
- First-episode nonprimary infection is when initial genital infection occurs in individuals with clinical or serologic evidence of prior HSV (usually HSV-1) infection.
- Recurrent infection occurs when appearance of genital lesions occurs at some time following healing of first-episode infection.

CLINICAL PRESENTATION

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- A summary of the clinical presentation of genital herpes is provided below.
- Incubation period: 2–14 days (mean, 4 days).
- Signs and symptoms:
    - ✓ First-episode infections:
        - Most primary infections are asymptomatic or minimally symptomatic.
        - Multiple painful pustular or ulcerative lesions on external genitalia developing over a period of 7–10 days; lesions heal in 2–4 weeks (mean, 21 days).
        - Flu-like symptoms (eg, fever, headache, malaise) during first few days after appearance of lesions.
        - Others—local itching, pain, or discomfort; vaginal or urethral discharge, tender inguinal adenopathy, paresthesias, urinary retention.
        - Severity of symptoms greater in females than in males.
        - Symptoms are less severe (eg, fewer lesions, more rapid lesion healing, fewer or milder systemic symptoms) with nonprimary infections.
        - Symptoms more severe and prolonged in immunocompromised patients.
        - Viral shedding lasts approximately 11–12 days for primary infections and 7 days for nonprimary infections.
    - ✓ Recurrent:
        - Prodrome seen in approximately 50% of patients prior to appearance of recurrent lesions; mild burning, itching, or tingling are typical prodromal symptoms.
        - Compared to primary infections, recurrent infections are associated with (1) fewer lesions that are more localized, (2) shorter duration of active infection (lesions heal within 7 days), and (3) milder symptoms.
        - Severity of symptoms greater in females than in males.
        - Symptoms more severe and prolonged in immunocompromised patients.
        - Viral shedding lasts approximately 4 days.
        - Asymptomatic viral shedding is more frequent during the first year after infection with HSV.
- Primary infections caused by HSV-1 and HSV-2 are virtually indistinguishable.
- Complications from genital herpes infections result from both genital spread and autoinoculation of the virus and occur most commonly with primary first episodes. Lesions at extragenital sites, such as the eye, rectum, pharynx, and fingers, are not uncommon. Central nervous system involvement is seen occasionally and can take several forms, including encephalitis, aseptic meningitis, and transverse myelitis. A major concern is the effect of genital herpes on neonates exposed during pregnancy.
- Viral culture and HSV DNA detection with polymerase chain reaction assays (preferred) are primary modalities used to confirm the diagnosis of first-episode genital herpes.

TREATMENT

- Goal of Treatment: To relieve symptoms and to shorten the clinical course, prevent complications and recurrences, and decrease disease transmission.
- Specific treatment recommendations are given in **Table 44-6**.

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- Oral **acyclovir, valacyclovir**, and **famciclovir** are the treatments of choice for outpatients with first-episode genital herpes. All patients with first-episode genital herpes should receive systemic antiviral therapy to prevent severe or prolonged symptoms associated with newly acquired infections.
- Suppressive with oral antiviral agents reduces the frequency and the severity of clinical episodes and asymptomatic shedding in 70%–80% of patients experiencing frequent recurrences.
- Acyclovir, valacyclovir, and famciclovir have been used to prevent reactivation of infection in patients seropositive for HSV who undergo transplantation procedures or induction chemotherapy.
- The safety of famciclovir and valacyclovir therapy during pregnancy is not well established, although experience with both agents in animal studies suggests a low risk of fetal harm. Acyclovir has been used in pregnant patients and has produced no evidence of teratogenicity.

TABLE 44-6

Treatment of Genital Herpes

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Type of Infection	Recommended Regimens[a,b]	Alternative Regimen
First clinical episode of genital herpes[c]	Acyclovir 400 mg orally three times daily for 7–10 days[d] *or* Famciclovir 250 mg orally three times daily for 7–10 days[d] *or* Valacyclovir 1 g orally twice daily for 7–10 days[d]	Acyclovir 5–10 mg/kg IV every 8 hours for 2–7 days or until clinical improvement occurs, followed by oral therapy to complete at least 10 days of total therapy[e]
Recurrent Infection		
Episodic therapy	Acyclovir 800 mg orally twice daily for 5 days[f] *or* Acyclovir 800 mg orally three times daily for 2 days[f] *or* Famciclovir 125 mg orally twice daily for 5 days[f] *or* Famciclovir 1 g orally twice daily for 1 day[f] *or* Famciclovir 500 mg orally once, followed by 250 mg orally twice daily for 2 days[f] *or* Valacyclovir 500 mg orally twice daily for 3 days[f] *or* Valacyclovir 1 g orally once daily for 5 days[f]	
Suppressive therapy[g]	Acyclovir 400 mg orally twice daily *or* Famciclovir 250 mg orally twice daily[h] *or* Valacyclovir 500 mg or 1000 mg orally once daily[i]	

CDC, Centers for Disease Control and Prevention; HIV, human immunodeficiency virus; HSV, herpes simplex virus; IV, intravenous.

[a]Recommendations are those of the CDC.

[b]HIV-infected patients can require more aggressive therapy.

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[c]Primary or nonprimary first episode.

[d]Treatment duration can be extended if healing is incomplete after 10 days.

[e]Only for patients with severe symptoms or complications that necessitate hospitalization. HSV encephalitis requires 21 days of IV therapy.

[f]Requires initiation of therapy within 24 hours of lesion onset or during the prodrome that precedes some outbreaks.

[g]Consider discontinuation of treatment after 1 year to assess frequency of recurrence.

[h]Famciclovir appears less effective for suppression of viral shedding.

[i]Valacyclovir 500 mg appears less effective than other valacyclovir and acyclovir regimens in patients with 10 or more recurrences per year.

TRICHOMONIASIS

- Trichomoniasis is caused by *T. vaginalis*, a flagellated, motile protozoan that was responsible for 6.9 million cases in the United States in 2018. *T. vaginalis* is primarily transmitted through sexual contact.
- Coinfection with other STIs (eg, gonorrhea) is not unusual, and the inflammatory response produced by trichomoniasis increases the risk of acquiring HIV.

CLINICAL PRESENTATION

- The typical presentation of trichomoniasis in men and women is presented below.
- Incubation period: 3–28 days. The organism can be detectable within 48 hours after exposure to infected partner.
- Most common sites of infection are the urethra (males) and endocervical canal (females); other sites of infection: rectum (usually caused by rectal intercourse in MSM), oropharynx, eye in males and urethra, rectum (usually caused by perineal contamination), oropharynx, eye in females.
- Symptoms:

  ✓ Males: Can be asymptomatic (more common in males than females) or minimally symptomatic; urethral discharge (clear to mucopurulent); dysuria, pruritus.

  ✓ Females: Can be asymptomatic or minimally symptomatic; scant to copious, typically malodorous vaginal discharge (50%–75%) and pruritus (worse during menses); dysuria, dyspareunia.
- Signs: Urethral discharge (males), vaginal discharge, vaginal pH 4.5–6, inflammation/erythema of vulva, vagina, and/or cervix, urethritis (females).
- Complications:

  ✓ Males: Epididymitis and chronic prostatitis (uncommon); male infertility (decreased sperm motility and viability).

  ✓ Females: PID and associated complications (ie, ectopic pregnancy, infertility); premature labor, premature rupture of membranes, and low-birth-weight infants (risk of neonatal infections is low); cervical neoplasia.
- *T. vaginalis* produces nonspecific symptoms also consistent with bacterial vaginosis; thus, laboratory diagnosis is required.
- The simplest and most reliable means of diagnosis is a wet-mount examination of the vaginal discharge. Trichomoniasis is confirmed if characteristic pear-shaped, flagellating organisms are observed. NAATs are highly sensitive and specific and are the preferred diagnostic method. Rapid point-of-care tests are also readily available, allowing for office-based testing.

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TREATMENT

- Goal of Treatment: To achieve cure of the infection, relief of symptoms, and prevent reinfection and transmission.
- Recommended and alternative treatment regimens for *T. vaginalis* include either **metronidazole** or **tinidazole,** both of which produce high cure rates.
- Treatment recommendations for *Trichomonas* infections are given in **Table 44-7**.
- To achieve maximal cure rates and prevent relapse with the single 2-g dose of metronidazole, simultaneous treatment of infected sexual partners is recommended.
- In patients who fail to respond to an initial course of metronidazole therapy, a second course of therapy with metronidazole 500 mg twice daily for 7 days is recommended.
- The CDC guidelines do not link metronidazole use with the potential for a disulfiram-like reaction in those that consume alcohol concurrently.
- Because metronidazole is secreted in breast milk, it is recommended that breast-feeding be interrupted for 12–24 hours after maternal ingestion of a single 2-g dose. Some clinicians prefer to delay treatment in women in the first trimester; however, metronidazole is a pregnancy category B drug and may be used for treatment in any trimester. Tinidazole is a pregnancy category C drug and should be avoided. However, the CDC now recommends that all symptomatic pregnant women, regardless of pregnancy stage, be tested and considered for treatment with metronidazole.
- Retesting for *T. vaginalis* is recommended for all sexually active women within 3 months following initial treatment due to the high rates of reinfection. Concurrent treatment of all sex partners is critical to ensure relief of symptoms and prevent reinfection and transmission.
- When patients remain symptomatic, it is important to ensure patient adherence and to determine if reinfection has occurred. In these cases, a repeat course of therapy, including treatment of sexual partner(s), is indicated.

TABLE 44-7

Treatment of Trichomoniasis

Type	Recommended Regimens[a]	Alternative Regimen
Symptomatic and asymptomatic infections	Women: Metronidazole 500 mg orally two times daily for 7 days[a,b,c] Men: Metronidazole 2 g orally in a single dose[b,d]	Tinidazole 2 g orally in a single dose
Persistent or recurrent infections	Metronidazole 2 g orally once daily for 7 days or tinidazole 2 g orally once daily for 7 days	
Treatment in pregnancy	Metronidazole 500 mg orally twice daily for 7 days	

[a]Recommendations are those of the CDC.

[b]Metronidazole labeling approved by the FDA does not include this regimen. Dosage regimens for treatment of trichomoniasis included in the product labeling are the single 2-g dose; 250 mg three times daily for 7 days; and 375 mg twice daily for 7 days. The 250-mg and 375-mg dosage regimens are currently not included in the CDC recommendations.

[c]For men, data are lacking for alternative treatment regimens and regimens for persistent infection. Consult an infectious diseases specialist.

[d]Randomized controlled trial comparing metronidazole 500 mg twice daily for 7 days and a single 2-g dose in women found fewer treatment failures in the 7-day regimen.

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OTHER SEXUALLY TRANSMITTED INFECTIONS

- Several STIs other than those previously discussed occur with varying frequency in the United States and throughout the world. Although an in-depth discussion of these diseases is beyond the scope of this chapter, recommended treatment regimens are given in **Table 44-8**.

TABLE 44-8

Treatment Regimens for Miscellaneous STIs

Infection	Recommended Regimens[a]	Alternative Regimens
Cervicitis[b]	Doxycycline 100 mg orally twice daily for 7 days	Azithromycin 1 g orally in a single dose
Epididymitis		
Acute infection most likely caused by *C. trachomatis* or *N. gonorrhoeae* Acute infection most likely caused by *C. trachomatis*, *N. gonorrhoeae*, or enteric organisms (men who practice insertive anal sex) Acute infection most likely caused by enteric organisms only	Ceftriaxone 500 mg IM in a single dose PLUS doxycycline 100 mg orally twice daily for 7 days Ceftriaxone 500 mg IM in a single dose PLUS levofloxacin 500 mg orally daily for 10 days Levofloxacin 500 mg orally daily for 10 days	
Lymphogranuloma venereum	Doxycycline 100 mg orally twice daily for 21 days[c]	Azithromycin 1 g weekly for 3 weeks or erythromycin base 500 mg orally four times daily for 21 days[c,d]
Nongonococcal urethritis (NGU)	Doxycycline 100 mg orally twice daily for 7 days	Azithromycin 1 g orally in a single dose or 500 mg orally in a single dose followed by 250 mg daily for 4 days
NGU (persistent or recurrent or due to *M. genitalium*)	Doxycycline 100 mg orally twice daily for 7 days followed by moxifloxacin 400 mg orally daily for 7 days	If azithromycin resistance can be ruled out, moxifloxacin may be substituted with oral azithromycin 1 g and then 500 mg daily for 3 days
HPV Infection		
External genital/perianal warts	*Provider-Administered Therapies:* Cryotherapy (eg, liquid nitrogen or cryoprobe); repeat weekly as necessary, *or* TCA 80%–90% *or* BCA 80%–90% applied to warts; repeat weekly as necessary, *or* Surgical removal (tangential scissor excision, tangential shave excision, curettage, or electrosurgery) *Patient-Applied Therapies:* Podofilox 0.5% solution or gel applied twice daily for 3 days, followed by 4 days of no therapy; cycle is repeated as	

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	necessary for up to four cycles. Imiquimod 3.75% or 5% cream applied at bedtime three times weekly for up to 16 weeks,[e,f] *or* Sinecatechins 15% ointment applied three times daily for up to 16 weeks	
Vaginal and anal warts	Cryotherapy with liquid nitrogen, or TCA or BCA 80%–90% as for external HPV warts; repeat weekly as necessary Surgical removal (not for vaginal or urethral meatus warts)	
Urethral meatus warts	Cryotherapy with liquid nitrogen or surgical removal	
Prevention (ages 9–14 years)[f]	Gardasil9 (HPV 9-valent [types 6, 11, 16, 18, 31, 33, 45, 52, 58]) recombinant vaccine 0.5 mL IM on day 1; a second dose administered 6–12 months following the first dose	
Prevention (age ≥15–26 years)[f]	Gardasil (HPV 9-valent [types 6, 11, 16, 18, 31, 33, 45, 52, 58]) recombinant vaccine 0.5 mL IM on day 1; a second and third dose are administered 1 and 6 months following the first dose	
Mpox Infection		
Treatment of severe or complicated mpox cases in patients with severely immunocompromised conditions[g]	Tecovirimat (TPOXX, ST-246) 600 mg (3 capsules) twice daily for 14 days if 40-120 kg (if >120 kg, 600 mg three times daily; if 25-40 kg, 400 mg twice daily)	Brincidofovir vaccinia immune globulin intravenous (VIGIV) Cidofovir
Prevention	Smallpox/monkeypox vaccine (JYNNEOS) two doses 28 days apart (0.5 mL subcutaneous) or (0.1 mL intradermally)	

BCA, bichloracetic acid; HPV, human papillomavirus; IM, intramuscular; TCA, trichloroacetic acid.

[a]Recommendations are those of the CDC.

[b]Consider concurrent treatment for gonorrhea infection if the patient is at risk for gonorrhea.

[c]Pregnant patients should be treated with erythromycin.

[d]If NGU is due to C. trachomatis, refer to treatment in Table 140-6, Chapter 140, DiPiro's Pharmacotherapy: A Pathophysiologic Approach, 12 ed. If NGU not due to C. trachomatis, consider HSV, trichomoniasis, M. genitalium, or HPV as potential causes of NGU and perform testing when appropriate.

[e]Safety during pregnancy is not established.

[f]CDC recommendations: vaccination is recommended in adolescents 11–12 years of age and can be given as early as age 9. Catch-up vaccination is recommended through age 26 years for those who either were not previously vaccinated or did not complete the vaccination series. Vaccination for adults ages 27–45 can be considered.

[g]Include ocular infections, neurologic complications, myopericarditis, complications associated with mucosal lesions, and complications from uncontrolled viral spread.

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See Chapter 145, Sexually Transmitted Infections, authored by Yvonne Burnett and Humberto Jimenez for a more detailed discussion of this topic.

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